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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,123	12/30/2003	David M. Gravett	110129.432	3283

41551 7590 09/12/2008

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
09/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/749,123	GRAVETT ET AL.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *154-172,241-244 and 246-255* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *154-172,241-244 and 246-255* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/20/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledged

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/20/2008 has been entered.

Status of Application

2. Acknowledgement is made of amendment filed on 06/20/2008. Upon entering the amendment, the claims 154 and 162 are amended and claim 245 cancelled. New claims 254-255 have been added. Accordingly, claims 154-172, 241-244 and 246-255 are pending and presented for examination.

Information Disclosure Statement

3. The Information Disclosure Statement filed on 06/20/2008 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office Action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 154-172, 241-244 and 246-255 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Applicant has amended claim 154 to recite "wherein the synthetic polymer is not admixture with any other synthetic polymer that is reactive with the synthetic polymer prior to applying the composition to the tissue or following applying the composition to the biological tissue". The phrase does not appear in the specification, or original claims as filed. Applicant does not point out specific basis for this limitation in the application, and none is apparent. The specification discloses that the composition does not contain any polymer that is reactive with the synthetic polymer (see page 3 lines 15-17). However, the specification does not recite "wherein the synthetic polymer is not admixture with any other synthetic polymer that is reactive with the synthetic polymer prior to applying the composition to the tissue or following applying the composition to the biological tissue".

Claim Objections

6. Claim 246 is objected to because of the following informalities: Claim 246 is dependent on canceled claim 245. Appropriate correction is required.

Response to Arguments

7. Applicant's arguments filed on 06/20/2008 have been fully considered but they are not persuasive. Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 154-157, 161,165, 166,168, 172, 241-246 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallace et al. (US 200110055615 A1).

With respect to claims 154-157, 161,165, 166 and 168, Wallace discloses a method of tissue repair and tissue related applications comprising a sulfhydryl reactive PEG compounds and succinimidyl reactive PEG compounds such as sulfhydryl-PEG/SG-PEG; sulfhydryl-PEG/SG-PEG/methylated (see para 0017-0020) suitable for use in tissue engineering application such as, tissue sealants, in tissue augmentation, in tissue repair, as hemostatic agent, in preventing tissue adhesion, in the prevention of surgical adhesion, in providing surface modifications, and in drug delivery application (see para 0066). And also tissue treatment polymeric composition comprising biologically active substance such as antibiotics, antineoplastic agents, antiangiogenic agents, and the like, suited for use in a variety of biological tissue related applications when rapid adhesion to the tissue and gel formation is desired (see abstract). And further the tissue treatment composition can be used for reducing the formation of adhesions after a surgical procedure in a patient by applying onto the damaged tissue or organ either by

spraying or by applying composition, to form a hydrogel on the tissue surface. The medical procedures include gynecological, abdominal, neurosurgical, cardiac, and orthopedic indications (see 0071). And further, composition can be applied as coatings to implants to affect the surface properties of implants or to help adhere implants to tissue surfaces e.g. catheters or breast implants to reduce or stop excessive fibrosis (see 0075).

With respect to claims 241-246, Wallace discloses tissue treatment composition comprising, synthetic polymer. Suitable synthetic hydrophilic polymer includes, polyalkylene oxide, such as polyethylene oxide and multifunctionally activated polyalkylene oxides, such as polyethylene glycol, (see 0039 and 0040). And also chain extenders or linking groups like alpha hydroxyl acids such as lactic acid and glycolic acid; poly(lactones) can be incorporated into one or both of the multifunctionally activated polymeric composition to provide a site for enzymatic degradation (e.g double-bonded carbon and carbonyl carbon would be anticipated to have this effect, see para 0047 and 0048).

Applicant's arguments filed on 06/20/2008 have been fully considered but they are not persuasive.

Applicant asserts that Wallace's composition comprises a two-component crosslinking synthetic polymer and is admixture with other synthetic polymer prior to applying the composition to the tissue.

This argument is not persuasive since the instant claim recites "a synthetic polymer and a drug, the synthetic polymer comprising poly(alkylene oxide)

functionalized with multiple activated groups Y" and Y is reactive with X. According to Wallace, two polymers were mixed to form single polymer, wherein the single polymer has multiple functional groups to react with X. Instant claims neither excludes nor recite how the single polymer comprising PEO is formed. Thus Wallace reference still meets the requirement of the instant claims.

10. Claims 154, 155, 161,169-172, 241-246 are rejected under 35 U.S.C. 102(b) as being anticipated by Rhee et al. (US 6,166,130).

With respect to claims 154 and 155, Rhee discloses a method for using the crosslinked polymer compositions to prevent the formation of surgical adhesions, as bioadhesives for tissue augmentation and also to coat a surface of a synthetic implant (see abstract). And also the crosslinked polymer composition comprise a synthetic polymer containing multiple nucleophilic and two or more electrophilic groups and/or biologically active agents such as growth factors may be delivered from the composition to a local tissue site in order to facilitate tissue healing and regeneration (The biological agents or active agents refers to organic molecules which exert biological effects in vivo, see column 15, line 34-40). And further, the crosslinked polymer composition can be used to coat tissues in order to prevent the formation of adhesions following surgery or injury to internal tissues or organs (e.g. the first and second synthetic polymers are mixed, then a thin layer of the reaction mixture is applied to the tissues comprising, surrounding, and/or adjacent to the surgical site before substantial crosslinking has occurred between the synthetic polymer).

With respect to claim 161, breast implants can be coated using the polymer composition in order to minimize capsular contracture (see column 20, line 45-47).

With respect to claims 169-172, Rhee discloses the method of using the crosslinked polymer compositions to block or fill various lumens and voids in the body of a mammalian subject. The crosslinked polymer compositions can also be coated onto the interior surface of a physiological lumen, such as a blood vessel or Fallopian tube, thereby serving as a sealant to prevent restenosis of the lumen following medical treatment, such as, balloon catheterization to remove arterial plaque deposits from the interior surface of a blood vessel or removal of scar tissue or endometrial tissue from the interior of a Fallopian tube (see column 21, line 1-20).

With respect to claims 241-246, Rhee discloses multifunctionally activated synthetic polymers capable of reacting with one another i.e., nucleophilic groups reacting with electrophilic groups, to form covalent bonds. Preferred multifunctionally activated polyethylene glycols for the use in the composition includes polyethylene glycols containing succinimidyl groups (see column 9, line 23-26). The backbone of each polymer is preferably a polyalkylene oxide, particularly ethylene oxide, propylene oxide, and mixture thereof. Examples of difunctional alkylene oxides can be represented by: X-polymer-X and Y-polymer-Y. The required functional groups X or Y is commonly coupled to the polymer backbone by a linking group "Q" (wherein Q = -O-(CH2)n-). An additional group, represented as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for e.g. for use in drug delivery application. The biodegradable groups "D" includes lactide,

glycolide, poly(alpha-hydroxy acid) and various di- or tripeptides (see column 5, line 1-55).

Applicant's arguments filed on 06/20/2008 have been fully considered but they are not persuasive.

Applicant asserts that Rhee's composition comprises a two-component gelling system and is admixture with other synthetic polymer prior to applying the composition to the tissue.

This argument is not persuasive since the instant claim recites "a synthetic polymer and a drug, the synthetic polymer comprising poly(alkylene oxide) functionalized with multiple activated groups Y" and Y is reactive with X. According to Wallace, two polymers were mixed to form single polymer, wherein the single polymer has multiple functional groups to react with X. Instant claims neither excludes nor recite how the single polymer comprising PEO is formed. And further Rhee discloses that multifunctionally activated synthetic polymers for use have been chemically modified (for example, PEG can be derivatized to form functionally activated PEG propion aldehdye, the tetrafunctionally activated form Fig 10; SG-PEG and SE-PEG shown in Figs 4-7) Thus Rhee reference still meets the requirement of the instant claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 154-172, 241-244 and 246-255 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al (US 2001/0055615 A1) or Rhee et al (US 6,166,130) or Trollsas et al (US 6,458,889 B1) in view of Greenwald et al (US 5,965,566) and Fischell et al (US 6,534,693 B2).

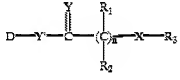
The teachings of Wallace and Rhee are stated above.

Trollsas teaches compositions of nucloephilic components and electrophilic components that crosslink in situ to form biocompatible crosslinked biomaterials (abstract, paragraph bridging col. 2 and 3). The compositions are useful for treating tissue augmentation, biologically active agent delivery, bioadhesion, and prevention of adhesions following surgery or injury (see abstract and col. 25 and 26). The compositions include materials such as PEG-thiol and PEG- succinimide (PEG-HNS). See Figure 19 and description thereof on col. 4, lines 37 - 39, and claim 50. PEG with primary amines is also used. See figures 1 - 15 and descriptions thereof. And the composition can be sued to coat the surface of any type of synthetic implant, particularly useful for implants where reduced thrombogenicity is an important consideration. The method may also be used to coat implantable surgical membranes, breast implants to

minimize capsular contracture (see col. 31 lines 13-22). And composition can also be used to coat onto the interior surface of a physiological lumen, such as a blood vessel or Fallopian tube, thereby serving as a sealant to prevent restenosis (see col. 31 lines 50-65).

Wallace, Rhee or Trollsas does not teach the combination of synthetic polymer and a drug such as cell cycle inhibitor (taxane) to further prevent the adhesion formation of biological tissue.

Greenwald discloses method of treatment of various medical conditions in mammal comprising a prodrug composition of biologically active compound (taxane derivatives) attached to the polymer of the formula:



Wherein: D is a residue of a biologically active moiety; X is an electron withdrawn group; Y and Y' are independently O or S; R_1 and R_2 are independently selected from groups consisting of H, C_{1-6} alkyls, aryls, substituted aryls, aralkyls, heteroalkyls, substituted heteroalkyls and substituted C_{1-6} alkyls: R_3 is a polyalkylene oxide (see abstract). And the biologically active compounds (taxol or paclitaxel), have been found to be effective anti-cancer agents and has been used systemically with efficacy in treating several human tumors, including ovarian, breast, and non-small cell lung cancer. And compositions (paclitaxel 2'PEG ester) are useful for treating neoplastic

disease, reducing tumor burden, preventing metastasis of neoplasms and preventing recurrences of tumor/neoplastic growth in mammals (see col. 15 lines 8-16).

Fischell discloses a sheet of material adapted for implantation between tissues of human body, the sheet of material including an attached anti-proliferative drug (rapamycin or taxol), the anti-proliferative drug being designed to prevent the formation of post-operative adhesions (see abstract). And anti-proliferative drug such as rapamycin or taxol which have a known effect on proliferating cells, the biodegradable mesh would decrease cellular proliferation and hence be a deterrent to the formation of adhesions. This mesh or guaze onto which the drug is attached may be placed within a generally cylindrical cavity of the human body to decrease scar tissue formation after a surgical procedure. Such a generally cylindrical cavity might be a nostril after an operation for a deviated septum, a fallopian tube, a billiary duct, a urethra, a ureter, a bronchial tube etc. (see col. 2 lines 1-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the paclitaxel loded in the synthetic polymer comprising poly(alkylene oxide) functionalized with multiple activated groups and their use to prevent the formation of surgical adhesions, as bioadhesives for tissue augmentation and also to coat a surface of a synthetic implant as taught by Wallace, Rhee or Trollsas, combine it with the composition comprising anti-proliferative drug such as (taxol) as taught by Grerenwald and Fishcell, and produce the instant invention.

One of the ordinary skill in the art would have been motivated to do this because Wallace, Rhee or Trollsas teaches compositions which are useful for treating tissue

augmentation, biologically active agent delivery, bioadhesion, and prevention of adhesions following surgery or injury.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 154, 155, 162, 241-244 and 247-255 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 18-21, 89-91, 93-95, 108, 110, and 131-141 of copending Application No.

10/749,117. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are drawn to a method of affecting biological processes in comprising: a composition consisting essentially of a synthetic polymer and a drug and claims of 10/747,117 are also drawn to a method for treating tissues comprising a biocompatible gel-forming drug-delivering composition. The difference between instant claims and those of 10/749,117 is that instant claims discloses synthetic polymer comprising PEG functionalized with multiple activated groups. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use different combination of polymers during the process of routine optimization, in order to enhance the method of affecting biological processes in vivo (tissue augmentation, biologically active agent delivery, bioadhesion, and prevention of adhesions following surgery or injury) because both are related to the same filed of endeavor, biocompatible gels that controllably release active agents and the combination would have yielded predictable results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

1. No claims are allowed at this time.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr